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New Quinoxalinyl Chalcone Derivatives: Search for Potent Antimicrobial Agents

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Abstract

Owing to the prevalence of antimicrobial resistance and its arising threat rendered by the ineffectiveness of existing antibiotics, the present work was aimed to generate new 5/6 substituted quinoxalinyl chalcones derivatives. A total of 16 compounds were synthesized and characterized by IR, ^{1}H NMR, ^{13}C NMR and mass spectral studies. The antimicrobial activity against resistant pathogens was by micro-dilution assay method. The result revealed that compounds bearing 2,4-dichloro benzylidine and 4-fluoro benzylidine moiety demonstrated promising antibacterial and antifungal activities against the selected pathogenic bacteria and fungi. It was observed that chalcones of 3,4-dihydroquinoxalin-2(1H)-one exhibited better activity (MIC: 2.57 μM) as compared to the chalcones of quinoxalin-2,3(1H,4H)-dione. The ClogP values of the synthesized compounds were in good agreement with antifungal activity indicated the significance of lipid solubility better cell wall penetration. Overall quinoxalinyl chalcones exhibited broad spectrum antimicrobial activity.

Keywords: 5/6 Quinoxalines; Chalcones; Drug resistant; Synthesis; Antibacterial; Antifungal activity

Introduction

Drug resistance was often observed with tuberculosis disease, but now it has percolated to other infections due to bacteria, virus, fungi, parasite etc. and evolved as "Antimicrobial resistance (AMR)". Antimicrobial resistance (AMR) is a serious threat to worldwide health that demands immediate solution from researchers because the expected mortality of infectious disease is not predictable unless newer agents are developed, especially to fight superbugs (resistant pathogens). AMR is a great challenge not only to developing counties but also to developed nations due to the huge cost and duration of antimicrobial treatment that will definitely affects the economy of people. Therefore, there is an urgent need to advance and to accelerate the antimicrobial research [1-3].

At this juncture, the reported antimicrobial activity for various oxoquinoxalines [4-6] and their diverse mechanism of action that could act as intercalating agents [7-11] have stimulated our team to design newer agents. In the light of literature and in continuation to our earlier reports [12-16], it was decided that oxoquinoxaline could be as better choice to produce new antibacterial scaffolds. Considering the present era of antimicrobial resistance and the underlying mechanism for resistance, it was our thought to design oxoquinoxaline with lipophilic side chain. As a result, aryl chalcone side chain was opted as side chain due to high lipophilic nature of benzylidine core. It is know that many existing antimicrobial molecules are ineffective for their poor cell wall permeability.

In the present work new chalcone derivatives were generated by exploiting 5 and 6 positions of quinoxaline through Friedel Crafts acylation followed by Claisen Schmidt condensation reactions. The obtained synthetic library was confirmed for its chemical structure by physical and spectral data and screened for antimicrobial activity against selected bacteria and fungi.

Materials and Methods

Purity of compounds was confirmed using precoated TLC and HPLC (Agilent LC 1200, C_{18} (250 mm × 4.6 mm, 5 μ) Column) techniques. The melting point was determined by open capillary tube method and is uncorrected. Functional groups were characterized by IR spectra using a Fourier transform-Infrared spectrophotometer (Alpha E, Bruker, ATR) technique) at resolution of 4 cm-1. The protons of the synthesized structures were assigned using proton nuclear magnetic resonance spectrum (^{1}H NMR) using a Varian VXR Unity using TMS as internal standard and DMSO-d_6/$CDCl_3$ as solvent). The mass spectrum from Shimadzu LCMS-2010A was used to confirm molecular weight. All the chemicals reagents used were of analytical or synthetic grade. Microorganisms used were ATCC strains and modified in laboratory as resistant species using ciprofloxacin and Griseofulvin respectively for bacteria and fungi [6].

Synthesis of Compounds

The starting material, quioxaline-2,3-dione(1) and 3,4-dihydroquinoxalin-2(1H)-one(4) were synthesized with reference to our earlier work [14,17].

Synthesis of 6-acetylquinoxaline-2,3(1H, 4H)-dione(2) and 5-acetylquinoxaline-2 (1H)-one (5)

A mixture of compound 1 or 4 (0.015 mol), anhydrous aluminium chloride (mol) and acetic anhydride (mol) were taken in a 5 ml microwave vial and irradiated in a microwave synthesizer at 110 watt for 1 minute. The reaction mixture was then cooled and poured onto crushed ice with stirring. The precipitated product was filtered on a

Buchner funnel under suction and washed with 3 × 10 ml portions of distilled water. The product was recrystallized from 95% ethanol.

Synthesis of 1-(3-substituted-1 oxo-2-propen-1-ylquinoxaline-2,3 (1H,4H)- diones) (3a-f) and 5-substituted quinoxalin-2(1H)-ones (6a-f)

Compound 2 or 5 (0.1 mol) was dissolved in 10% alcoholic sodium hydroxide. The reaction mixture was treated with various aldehydes (0.1 mol) and stirred overnight in an ice bath. The crude product was collected on a Buchner funnel and recrystallized from methanol to yield respective compounds.

Characterization of the Compounds

6-acetylquinoxaline-2,3(1H,4H)-dione (2): White crystals, IR (KBr pellet, cm^{-1}): 3326.47 (NH, amide), 3063.36 (C-H stretching, aromatic), 2953.32 (C-H stretching, aliphatic), 1715.40 (C=O stretching, amide), 1620.32 (C=O, ketone); ^{1}H NMR (DMSO–d_6, δ ppm): 12.12 (s, 1H), 11. 89 (s, 1H), 7.52-7.32 (m, 3H, Ar), 3.34 (s, 3H); MS (API-ES, m/z): 205.1 $(M+H)^+$.

6-cinnamoylquinoxaline-2,3(1H, 4H)-dione (3a): White needles, IR (KBr pellet, cm^{-1}): 3241.25 (NH, amide), 3055.61 (C-H stretching, aromatic), 2928.12 (C-H stretching, aliphatic), 1713.53 (C=O stretching, amide), 1674.94 (C=O stretching, chalcone); ^{1}H NMR (DMSO–d6, δ ppm): 11.89 (s, 1H), 11.31 (s, 1H), 7.79 (d, J=15.6, 1H), 7.71 (d, J=15.6, 1H), 7.88-7.01 (m, 8H, Ar); MS (API-ES, m/z): 293.1 $(M+H)^+$.

6-(3-(4-nitrophenyl)acryloyl)quinoxaline-2,3(1H,4H)-dione (3b): Yellow crystals, IR (KBr pellet, cm^{-1}): 3234.53 (NH, amide), 3079.88 (C-H stretching, aromatic), 2933.21 (C-H stretching, aliphatic), 1718.52(C=O stretching, amide), 1679.83(C=O stretching, chalcone) 1595.54 (NO_2 stretching); ^{1}H NMR (DMSO–d_6, δ ppm): 11.94 (s, 1H), 10.9 (s, 1H), 7.79 (d, J=15.6, 1H), 7.41 (d, J=15.6, 1H), 7.45-7.05 (m, 7H, quinoxaline); MS (API-ES, m/z): 338.1 $(M+H)^+$.

6-(3-(2,4-dichlorophenyl)acryloyl)quinoxaline-2,3(1H,4H)-dione (3c): White needle crystals, IR (KBr pellet, cm^{-1}): 3334.27 (NH, amide), 3108.40 (C-H stretching, Ar), 1723.48 (C=O stretching, amide), 1681.46 (C=O stretching, chalcone), 759.45 (C-Cl stretching, aromatic); ^{1}H NMR (DMSO–d_6, δ ppm): 11.94 (s, 1H,CONH), 11.90 (s, 1H, CONH), 7.62 (d, J=15.2, 1H), 7.45 (d, J=15.2, 1H), 7.41-7.20 (m, 6H, Ar); MS (API-ES, m/z): 361.0 $(M+H)^+$.

6-(3-(4-(dimethylaminio)phenyl)acryloyl)quinoxaline-2,3(1H,4H)-dione (3d): White crystals, IR (KBr pellet, cm^{-1}): 3415.58 (NH, amide), 3058.75 (C-H stretching, aromatic), 2833.29 (C-H stretching, aliphatic), 1723.48 (C=O stretching, amide), 1678.73 (C=O stretching, chalcone); ^{1}H NMR (DMSO–d_6, δ ppm): 11.90 (s, 1H), 10.92 (s, 1H), 7.65 (d, J=15.2, 1H), 7.48 (d, J=15.2, 1H), 7.13-7.08 (7H, Ar), 2.99 (s, 6H); MS (API-ES, m/z): 336.2 $(M+H)^+$.

6-(3-(3,4,5-trimethoxyphenyl)acryloyl)quinoxaline-2,3(1H,4H)-dione (3e): White crystals, IR (KBr pellet, cm^{-1}): 3237.52 (NH, amide), 3055.51 (C-H stretching, aromatic), 2928.12 (C-H stretching, aliphatic), 1714.83 (C=O stretching, amide), 1674.94 (C=O stretching, chalcone); ^{1}H NMR (DMSO–d_6, δ ppm): 11.25 (s, 1H), 10.93 (s, 1H), 8.05 (d, J=15.6, 1H), 7.45 (d, J=15.6, 1H), 7.883-7.012 (5H, Ar), 3.90 (s, 3H), 3.84(s, 3H), 3.80 (s, 3H); MS (API-ES, m/z): 383.0 $(M+H)^+$.

6-(3-(4-fluorophenyl)acryloyl)quinoxaline-2,3(1H,4H)-dione (3f): Yellow crystals, IR (KBr pellet, cm^{-1}): 3291.74 (NH stretching), 3051.68 (C-H stretching, aromatic), 2970.84 (C-H stretching, aliphatic), 1721.48 (C=O stretching, amide), 1698.22 (C=O stretching, chalcone); ^{1}H NMR (DMSO–d_6, δ ppm): 12.095 (s, 1H), 11.224 (s, 1H), 7.70 (d, J=15.6, 1H), 7.64 (d, J=15.6, 1H), 7.121-7.144 (m, 7H, aromatic); MS (API-ES, m/z): 311.1 $(M+H)^+$.

Quinoxaline-2-one (4): Yellow crystals, IR (KBr, cm^{-1}): 3291.26 (NH stretching, amide), 3100.41 (C=H stretching, aromatic), 1715.23 (C=O stretching, amide), 1675.38 (C=O stretching, chalcone), 1578.43 (C=N strectcing, aromatic), 1515.52 (C=C stretching, aromatic); ^{1}HNMR (CDCl3, δ ppm): 11.541 (s, 1H), 7.012 - 7.812 (m, 5H, quinoxaline); MS (API-ES, m/z): 147.2 $(M+H)^+$.

5-acetylquinoxalin-2 (1H)-one (5): Yellow crystals, IR (KBr, cm^{-1}): 3267.11 (NH stretching, amide), 3077.25 (C=H stretching, aromatic), 1724.58 (C=O stretching, amide), 1678.32 (C=O stretching, ketone), 1573.51 (C=N strectcing, aromatic), 1523.68 (C=C stretching, aromatic); ^{1}HNMR ($CDCl_3$) δ: 10.670 (s, 1H), 7.010-7.491 (m, 4H), 3.311(s, 3H); MS (API-ES, m/z): 189.2 $(M+H)^+$.

5-(3-phenylacryloyl) quinoxalin-2 (1H)-one (6a): Yellow crystals, yield 64%, mp 199–200°C. IR (KBr) in cm^{-1}: 3267.11 (NH stretching, amide), 3082.57 (C=H stretching, aromatic), 1724.58 (C=O stretching, amide), 1689.13 (C=O stretching, chalcone), 1590.73 (C=N strectcing, aromatic), 1514.53 (C=C stretching, aromatic); ^{1}H NMR (DMSO–d_6, δ ppm): 11.921 (s, 1H), 7.212-7.824 (m, 9H, Ar), 7.49 (d, J=15.6, 1H), 7.41 (d, J=15.6, 1H); MS (API-ES, m/z): 277.1 $(M+H)^+$.

5-(3-(4-nitrophenylacryloyl) quinoxalin-2(1H)-one (6b): Brown crystals, IR (KBr, cm-1): 3221.28 (NH stretching, amide), 3077.13 (C=H stretching, aromatic), 1715.32 (C=O stretching, amide), 1694.27 (C=O stretching, chalcone), 1590.73 (C=N strectcing, aromatic), 1523.26 (NO_2 stretching), 1512.96 (C=C stretching, aromatic); ^{1}H NMR (DMSO–d_6, δ ppm): 10.70 (s, 1H), 7.31-8.11 (m, 8H, Ar), 7.57 (d, J=15.2, 1H), 7.43 (d, J=15.2, 1H); MS (API-ES, m/z): 322 $(M+H)^+$.

5-(3-(2,4-dichlorophenyl) acryloyl) quinoxalin-2 (1H)-one (6c): Yellow crystals, IR (KBr, cm-1): 3278.21 (NH stretching, amide), 3084.05 (C=H stretching, aromatic), 1715.32 (C=O stretching, amide), 1684.63 (C=O stretching, chalcone), 1582.96 (C=N strectcing, aromatic), 1519.14 (C=C stretching, aromatic); ^{1}H NMR (DMSO–d_6, δ ppm): 11.791 (s, 1H), 7.182-8.101 (m, 7H, Ar), 7.68 (d, J=15.6, 1H), 7.51 (d, J=15.6, 1H); MS (API-ES, m/z): 345.02 $(M+H)^+$.

5-(3-(4-(dimethylamino) phenyl) acryloyl) quinoxalin-2 (1H)-one (6d): Light brown crystals, IR (KBr, cm^{-1}): 3314.72 (NH stretching, amide), 3084.05 (C=H stretching, aromatic), 1720.54 (C=O stretching, amide), 1661.58 (C=O stretching, chalcone), 1573.14 (C=N strectcing, aromatic), 1522.42 (C=C stretching, aromatic); ^{1}H NMR (DMSO–d_6, δ ppm): 11.905 (s, 1H), 7.14-7.66 (m, 8H, Ar), 7.82 (d, J=15.4, 1H), 7.79 (d, J=15.4, 1H), 3.01 (s, 6H); MS (API-ES, m/z): 320.10 $(M+H)^+$.

5-(3-(3,4,5-trimethoxyphenyl) acryloyl) quinoxalin-2(1H)-one (6e): Brown crystals, IR (KBr, cm-1): 3297.16 (NH stretching, amide), 3092.61 (C=H stretching, aromatic), 1718.67 (C=O stretching, amide), 1693.31 (C=O stretching, chalcone), 1601.03 (C=N strectcing, aromatic), 1534.26 (C=C stretching, aromatic); ^{1}H NMR (DMSO–d_6, δ ppm): 10.71 (s, 1H), 7.1-7.6 (m, 6H, Ar), 8.01 (d, J=15.2, 1H), 7.85 (d, J=15.2, 1H), 3.96 (s, 3H), 3.92 (s, 3H), 3.90 (s, 3H); MS (API-ES, m/z): 367.08 $(M+H)^+$.

5-(3-(4-fluorophenyl)acryloyl)quinoxalin-2(1H)-one (6f): light orange crystals, IR (KBr, cm-1): 3254.21 (NH stretching, amide), 3068.57 (C=H stretching, aromatic), 1727.42 (C=O stretching, amide), 1673.52 (C=O stretching, chalcone), 1582.11 (C=N strectcing,

aromatic), 1526.31 (C=C stretching, aromatic); ^{1}H NMR (DMSO–d_6, δ ppm): 10.97 (s, 1H), 7.23-7.27 (m, 8H, Ar), 7.62 (d, J=15.2, 1H), 7.54 (d, J=15.2, 1H); MS (API-ES, m/z): 367.08 $(M+H)^+$.

Antimicrobial Screening

Antibacterial activity was performed against ciprofloxacin resistant species of *Staphylococcus aureus* ATCC 25923, *Escherichia coli* ATCC 25922, *Proteous vulgaris* ATCC 13315 and *Pseudomonas aeruginosa* ATCC 27853 by micro-dilution assay method (0.04-9.6 µg/ml).

In the same way antifungal activity was screened against griseofulvin resistant *Aspergillus niger* ATCC 16404 and *Candida albicans* ATCC 10231. The resistant species were produced in laboratory as per our earlier report [6].

The obtained MIC (90% inhibition) was converted into micromolar concentration (µM). The above antifungal and antibacterial activities were performed as per the literature [12,13].

Results

The synthetic figure adopted was quite convenient and afforded pure compounds. A total of 14 compounds were obtained from Figure 1. The chalcones 3(a-f) was yellowish in nature with yield range from 50-70% whereas the chalcones 6(a-f) was cream colored crystals with yield ranging from 60-82%. All the melting point was above 300°C. The R_f value of the compounds were 0.4 to 0.8.

All the compounds were relatively stable and none were found to be hygroscopic or deliquescent. The physical data of the compounds were shown in Table 1. The spectral data of the compounds illustrated in Figure 1 were satisfactory for the proposed structures. The data related to spectral interpretation is detailed in materials and methods section.

The antimicrobial activity was carried out against four bacteria and two fungi and the activities were measured by minimum inhibitory concentration (MIC in µM) using microdilution assay method. The standards used were ciprofloxacin (CIP) and griseofulvin (GSFN) for antibacterial and antifungal activity respectively.

DMSO was employed as solvent blank. The results of antibacterial and antifungal activities revealed that all the chalcones exhibited considerable antibacterial and antifungal activities when compared to the intermediates (compounds 2 and 5).

The most active compounds against *Staphylococcus aureus* and *Escherichia coli* (Gram positive bacteria) were compounds 6e and 6f with MIC of 3.27 µM and 2.57 µM respectively. The compound 6e was found to be the most active compound against *Proteus vulgaris* and *Pseudomonas aerugenosa* (Gram-negative bacteria) with MIC of 3.27 µM. In the case of anti-fungal screening, compound 6c was found to be the most active against the *Asperigillus niger* and *Candida albicans* with MIC of 1.85 µM.

Discussion

The synthetic Figure was consisted of two routes respectively for 3a-f and 6a-f as shown in Figure 1. The product formation and the reaction progress were monitored by TLC technique. The starting materials used were quinoxaline 2, 3 (1H, 4H)–dione 1 and 3, 4-dihydroquinoxalin-2(1H)-ones 4 respectively for 3a-f and 6a-f.

The intermediate in both routes was acetyl derivatives (compound 2 and 3). The acetylation of compound 1 and 4 afforded compound 2 and 5, respectively and the reaction was confirmed by the presence of aliphatic proton NMR signal (-CH3 at ~3 ppm).

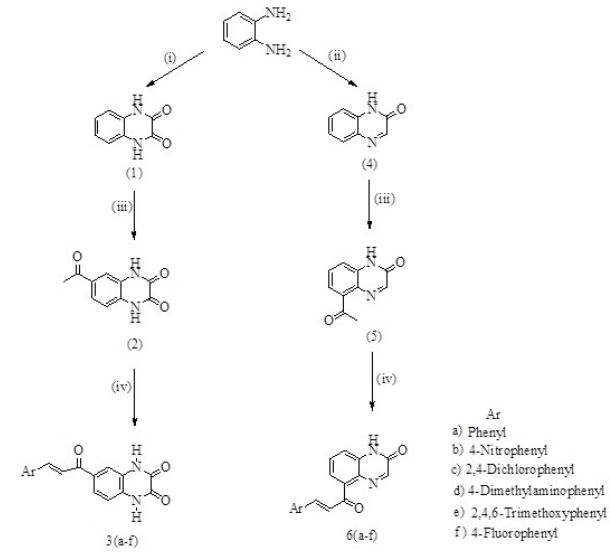

Figure 1: Reaction conditions (i) Oxalic acid/4N HCl/ MWI (ii) α-Chloroacetylchloride/ 1N NaOH/MWI; (iii) Acetic anhydride/ $AlCl_3$/MWI; (iv) Ar-CHO/Alc. NaOH/stirring at RT.

Further the formation of chalcones (3a-f and 6a-f) respectively from compound 2 and 5, were confirmed by two proton NMR signals accounting for unsaturated –CH=CH- system (at ~7-8 ppm). The J-value (~ 15 Hz) of doublets for protons of –CH=CH- system indicated the E configuration. All the compounds were obtained as stable crystals except compound 2 and 3. The yields of all chalcones were more than 60% and were colored in nature (yellowish to reddish).

The retardation factor (R_f value) and ClogP for all chalcones were more than intermediate and starting materials. It indicated that the prepared chalcones are more lipophilic in nature.

The melting points were found to be more than 200°C; this could be due to considerable intermolecular forces. The physical data of the synthesized compounds are shown in Table 1 Structures of the compounds were confirmed by IR, ^{1}HNMR, and mass spectral data.

All above compounds were screened for antibacterial and antifungal activities and their results were tabulated in Table 2. Screening was performed using micro-dilution assay method and result was obtained as minimum inhibition concentration (MIC_{90} in micro-molar concentration).

The result revealed that chalcones exhibited promising and broad spectrum activity against tested species as compared to the intermediates (>12 µM) and starting materials (>30 µM). It was noted that acetyl derivatives of quinoxalines are more active against gram positive than Gram negative bacteria.

However 3,4–dihydroquinoxalin-2(1H)-one 4 and its acetyl derivatives 5 demonstrated 2 times more potent antimicrobial actvities than quinoxaline–2,3(1H,4H)- dione 1 and its acetyl derivatives 2. All chalcones were 5-10 times more potent than starting materials indicated the new scaffolds are quite acceptable for antimicrobial drug design.

Comp. code	Mol. formula	Mol. Wt	m.p (°C)	% yield	R_f value	ClogP
1	$C_8H_6N_2O_2$	162.15	>300	70.82	0.83	-0.292
2	$C_{10}H_8N_2O_3$	204.18	262-264	60	0.71	-0.853
3a	$C_{17}H_{12}N_2O_3$	292.29	>300	69.6	0.58	1.190
3b	$C_{17}H_{11}N_3O_5$	337.29	>300	71.2	0.52	0.933
3c	$C_{17}H_{10}Cl_2N_2O_3$	361.18	>300	67.5	0.49	2.616
3d	$C_{19}H_{17}N_3O_3$	335.36	>300	71.9	0.64	1.355
3e	$C_{20}H_{18}N_2O_6$	382.37	>300	68.4	0.42	1.190
3f	$C_{17}H_{11}FN_2O_3$	310.28	>300	65.8	0.61	1.333
4	$C_8H_6N_2O$	146.15	230-231	68	0.46	0.305
5	$C_{10}H_8N_2O_2$	188.18	243-245	57	0.58	0.067
6a	$C_{17}H_{12}N_2O_2$	276.29	199-200	64	0.38	2.110
6b	$C_{17}H_{11}N_3O_4$	321.29	291-293	57	0.51	1.853
6c	$C_{17}H_{10}N_2O_2Cl_2$	345.18	>300	61	0.42	3.536
6d	$C_{19}H_{17}N_3O_2$	319.36	250-252	47	0.72	2.275
6e	$C_{20}H_{18}N_2O_5$	366.37	>300	52	0.8	2.110
6f	$C_{17}H_{11}FN_20_2$	249.28	>300	46	0.74	2.253
m.p: Melting point; R_f: Retardation factor in TLC						

Table 1: Physical data of the compounds.

Comp. Code	Antibacterial activity MIC_{90} (in µM)				Antifungal activity MIC_{90} (in µM)	
	S. aureus	*E. coli*	*P. vulgaris*	*P. aeruginosa*	*A. niger*	*C. albicans*
1	>59.20	>59.20	>59.20	>59.20	>59.20	>59.20
2	23.51	23.51	>47.02	>47.02	>47.02	23.51
3a	8.21	8.21	4.1	8.21	>32.84	>32.84
3b	7.11	7.11	7.11	7.11	>28.46	>28.46
3c	3.32	6.64	6.64	6.64	3.32	3.32
3d	3.59	3.59	7.52	7.52	14.31	14.31
3e	6.28	6.28	6.28	6.28	12.55	12.55
3f	3.88	7.73	7.73	3.87	7.73	3.87
4	32.84	32.84	32.84	32.84	>65.69	>65.69
5	12.75	25.51	25.51	25.51	25.51	25.51
6a	8.69	4.34	8.67	8.69	8.69	17.37
6b	7.47	7.47	7.47	7.47	7.47	7.47
6c	3.71	3.71	3.71	3.71	1.85	1.85
6d	3.76	7.51	3.76	3.76	3.76	3.76

6e	3.27	3.27	3.27	3.27	3.27	3.27
6f	5.13	2.57	5.13	5.13	5.13	2.57
CIP	1.93	0.96	3.65	1.97	--	--
GSFN	--	--	--	--	0.64	0.64
Blank	--	--	--	--	--	--
CIP: Ciprofloxacin; GSFN: Griseofulvin						

Table 2: Antimicrobial activity of compounds by micro-dilution assay.

Among all chalcones, 6a-f series were relatively more potent than 3a-f. It might be due to high lipophilicity. Out of all chalcones, compound 6c, 6d and 6e were found to be more potent against both bacteria (3.27-3.71 µM) and fungi (3.27-1.85 µM).

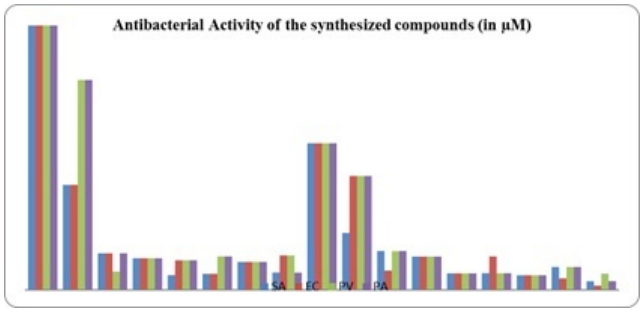

Figure 2: Antibacterial activity (MIC90) of the synthesized compounds (X-axis: compound code; Y-axis: antibacterial potency in micromoles; SA: *Staphylococcus aureus*; EC: *E. coli*; PV: *Proteus vulgaris*; PA: *Pseudomonas aeruginosa*; CIP: Ciprofloxacin).

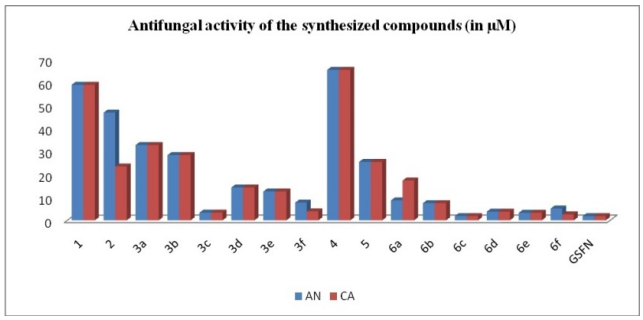

Figure 3: Antifungal activity (MIC_{90}) of the synthesized compounds (X-axis: compound code; Y-axis: antifungal potency in micromoles; AN: *Asperigillus niger*; CA: *Candida albicans*; GSFN: Griseofulvin).`

This indicates the importance of substitution on benzylidine part of chalcones where substitution on phenyl moiety increases the potency to 2-3 times as compared to unsubstituted compound 3a and 6a. 2,4,6-trimethoxy substitution (compound 3e and 6e) was found to equally active against both Gram Positive and negative species. Among all, 2, 4-dichloropheyl/4 fluorophenyl substituted compounds (3c, 6c, 3f, 6f) were relatively more active against fungi than bacteria. The most potent compound of the series was 6c (dichlorophenyl substitution). Relative potency of the synthesized compounds can be observed from Figure 2 and 3.

Conclusions

Thus halogen substituted chalcones of quinoxaline (electron withdrawing) can be considered for development of antifungal agents whilst amino/and methoxy substitution (electron releasing) may be considered for development of antibacterial agents. Nitro substitution did not show any significant increase in antimicrobial spectrum.

Conflict of Interest

All authors expressed no conflict of interest.

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